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The cascade of care for opioid use disorder: a retrospective study in British Columbia, Canada

Running Head: The cascade of care for opioid use disorder

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Abstract:

Background and Aims: The ‘cascade of care’ framework, measuring attrition at various stages of care engagement, has been proposed to guide the public health response to the opioid overdose public health emergency in British Columbia (BC), Canada. We estimated the cascade of care for opioid use disorder and identified factors associated with care engagement for people with opioid use disorder (PWOUD) provincially.

Design: Retrospective study using a provincial-level linkage of four health administrative databases.

Setting and participants: All PWOUD in BC from January 1st, 1996 to November 30th, 2017.

Measurements: The eight-stage cascade of care included diagnosed PWOUD, ever on opioid agonist treatment (OAT), recently on OAT, currently on OAT, and retained on OAT: $\geq 1m$, $\geq 3m$, $\geq 12m$, $\geq 24m$). Health care use, homelessness and other demographics were obtained from physician billing records, hospitalizations and drug dispensation records. Receipt of income assistance was indicated by enrollment in Pharmacare Plan C(48).

Findings: A total of 55,470 diagnosed PWOUD were alive at end of follow-up. As of 2017, a majority of the population (N=39,456; 71%) received OAT during follow-up; however, only 33% (N=18,519) were currently engaged in treatment and 16% (N=8,960) had been retained for at least one year. Compared with those never on OAT, those currently engaged in OAT were more likely to be under 45 years of age (adjusted odds ratio: 1.75; 95% confidence interval: 1.64,1.89), male (1.72; 1.64,1.82), with concurrent substance use disorders (2.56; 2.44,2.70), HCV (1.22; 1.14,1.33) and either homeless or receiving income-assistance (4.35; 4.17,4.55). Regular contact with the healthcare system – either in outpatient or acute care settings – was common among PWOUD not engaged in OAT regardless of time since diagnosis or treatment discontinuation.

Conclusions: People with opioid use disorder in British Columbia, Canada show high levels of outpatient care prior to diagnosis. Younger age, male sex, urban residence, lower income level, and homelessness appear to be independently associated with increased opioid agonist treatment engagement.

Introduction

In the midst of the rising burden in opioid-related morbidity and mortality in North America, an unprecedented 3,998 opioid-related deaths occurred in Canada in 2017, representing a 33% increase from the previous year(1). In the first six months of 2018, the nation observed an additional 2,066 opioid-related deaths(1). These increases in overdose mortality are largely attributed to contamination of the illicit drug supply with fentanyl and its analogues(2). In the province of British Columbia (BC) an estimated 1,514 illicit drug overdoses deaths occurred in 2018 (rate 30 per 100,000); up 53% from 2016 (992 deaths, rate 20 per 100,000) accounting for the highest provincial opioid-related death rate in Canada(1, 3).

Numerous studies have demonstrated that opioid agonist treatment (OAT), primarily with methadone or buprenorphine, is effective for the treatment of opioid use disorder (OUD)(4-8). Prolonged retention on treatment has been associated with substantial reductions in opioid-related morbidity and mortality(9-13), illicit drug use, criminal activity, and high risk behaviors that increase the risk of transmitting or acquiring HIV and HCV(6, 14). Most importantly, engagement in OAT is estimated to reduce the relative risk of all-cause mortality by a factor of 3.2 on methadone and 2.2 on buprenorphine, making increased OAT access, quality, and expanded treatment options a cornerstone in the response to the opioid overdose crisis across the continent(2, 14-17). Numerous provincial initiatives have been implemented to increase OAT access, particularly following the provincial declaration of a public health emergency in April 2016. Furthermore, one BC prospective cohort study reported only over a third of their participants with OUD were retained in OAT in 2016, signaling an urgent need to improve OAT engagement and retention(18).

Ongoing monitoring of the quality of addiction care and care engagement can provide a powerful basis to assess the success of efforts to close the implementation gap between research evidence and access to evidence-based addiction care(19, 20). However, engagement in care varies greatly across geographic regions, and within people with distinct demographic characteristics and healthcare needs(21). In BC, substantial increases in OAT engagement were identified since 2006 that differed by socio-demographic characteristics, comorbidities and

social-structural exposures; however, engagement and access by area of residence as well as health care service utilization were not investigated(18). Furthermore, in 2018, another BC study documented higher rates of hospitalizations and community physician visits among people who had experienced an overdose(22). It is clear that information on the characteristics of diagnosed people with opioid use disorder (PWOUD) never engaging in OAT and those who have engaged in OAT but are no longer receiving treatment are key to informing targeted strategies toward improving OAT engagement and retention and identifying missed opportunities for treatment.

The concept of a 'cascade of care', measuring attrition at various stages of engagement in the treatment system has become a focal point for implementation efforts in HIV/AIDS (23-26) with more recent applications to Hepatitis C Virus (HCV)(27) and diabetes(28). The concept has been proposed to guide the public health response towards the opioid crisis(29-31). Our objectives were to generate a cascade of OUD care using linked individual-level data for all PWOUD accessing care in BC and identify factors associated with OAT engagement.

Methods

Study setting

Since the establishment of BC's OAT program in 1996, OAT access has expanded rapidly(32). For BC residents, OAT and OUD-related medical care are either fully publicly funded based on income, or partially covered(33). Since 2015, buprenorphine/naloxone has been included as a regular health care benefit(34). The most commonly used forms of OAT in BC, methadone and buprenorphine/naloxone can be prescribed by primary physicians and dispensed via community-based pharmacies(35, 36). Since mid-2017, alternative forms of OAT including slow-release oral morphine and injectable OAT have also been offered in these low-threshold settings(37).

Study design

We conducted a retrospective study utilizing a provincial-level linkage of four health administrative databases (Supplementary Appendix A1-A2) to define the population of BC residents with OUD from January 1st, 1996 to November 30th, 2017. The PharmaNet database(38) (OAT dispensations), the Discharge Abstract Database(39) (DAD; hospitalizations), the Medical Services Plan database(40) (MSP; physician billing records), and BC Vital Statistics(41) (deaths and their underlying causes) were linked via de-identified individual study IDs with complete data to the end of study follow-up for PharmaNet and Vital Statistics, and up to March 30th 2016 for MSP and November 2nd 2017 for DAD datasets (Supplementary Appendix Figure A1). We used case-finding algorithms to identify the population of individuals who had ever accessed health services for OUD, acknowledging the possible misclassification in outpatient and hospital ICD-9/10 codes used to identify OUD (Supplementary Appendix A1.5).

Individuals were followed from the first record of OUD to either administrative loss to follow-up or death. To account for out-of-province migration, administrative loss to follow-up was defined as no record of any kind in any of the linked databases for at least 66 months prior to the end of study follow-up. The 66-month cut-off was determined empirically based on the distribution of

gaps between records of hospitalizations, physician billing records, and drug dispensations over the full duration of follow-up (Supplementary Appendix A2.2).

Key measures

The OUD Cascade of Care

We defined an eight-stage OUD cascade of care, focused on stages from diagnosis to long-term retention in OAT, directly drawn from our linked provincial administrative datasets as of the end of each calendar year (excluding 2017, end of follow-up: November 31st 2017). Detailed definitions of the cascade stages are provided in **Table 1** and described further in Supplementary Appendix A1. PWOUD who discontinued OAT excluded PWOUD who had completed OAT dose tapering (for MET defined as $\leq 5\text{mg/day}$; BNX: $\leq 2\text{mg/day}$ on the last day of OAT receipt), with no subsequent record of OUD-related hospitalization or OAT re-entry.

Demographics & Clinical History

We described PWOUD disaggregated according to covariates known to influence engagement in healthcare(18, 42, 43). Covariates included: age (<25, 25-34, 35-44, ≥ 45 years); region of health service delivery area (HSDA; rural or urban); sex (male or female); and diagnoses of comorbid conditions (alcohol use disorder, other substance use disorders (not including OUD), mental health conditions, HIV, HCV, and non-cancer chronic pain). Comorbid conditions were attributed using ICD-9/10 codes in physician billing and hospitalization records (Supplementary Appendix A1.5). For PWOUD diagnosed during 2012 to 2016, we additionally indicated the source of initial OUD-related contact (hospitalization, outpatient care, or OAT dispensation); and receipt of OAT within 3 months of diagnosis(44-46). Region of HSDA was based on the BC Ministry of Health's categories of geographic service areas (GSA; metro, urban/rural, rural, and remote)(47). Finally, receipt of income assistance was indicated by enrollment in Pharmacare Plan C(48), and homelessness was indicated by ICD9/10 codes in inpatient and outpatient records (Supplementary Appendix A1.6).

Health service utilization

We measured all-cause health service utilization from April 1st 2015 to March 31st 2016, among PWOU not engaged in OAT by time since OAT discontinuation or OUD diagnosis to March 31st 2016 (>5 years, 1-5 years, <1 year). This period was chosen as physician billing records (outpatient care) were available only until March 31, 2016. Individual contacts within the health care system were summarized as follows: (1) no contact (no record in any database), (2) outpatient care only – low intensity, (3) outpatient care only – high intensity, (4) one hospitalization, and (5) more than one hospitalization. Low intensity outpatient care was defined as having both physician billing records and drug dispensation days lower than the baseline cohort's third quartile (i.e. Q3). High intensity outpatient care only was defined as having either physician billing records, or drug dispensations higher than Q3.

Statistical analyses

We first plotted the OUD cascade of care from 2001 to 2017 (to allow for five years of data capture to establish OUD diagnosis), and provided population characteristics including health service utilization among PWOU newly diagnosed between 2012 and 2016. Temporal trends in care engagement were determined using the Cochran-Armitage test. Univariate comparisons were executed using chi-squared tests.

Finally, we constructed a multinomial regression model from 2001 to 2016 using generalized estimating equations (GEE) with an independent working correlation matrix to analyze factors associated with OAT engagement. Our response variable included cascade stages at three levels: "OUD diagnosed but never on OAT", "Ever on OAT but not currently on OAT", and "Currently OAT" from January 1st 2001 to December 31st 2016, measured at the end of each calendar year. The outcome was considered as nominal in the generalized logit model, assuming that odds ratios for any pair of the dependent variable categories are determined without reference to the other categories. Time-invariant variables included age group at the first OUD indication and sex. Time-variant variables included residence in a rural region, comorbidities, year since the first OUD indication, and ever homeless or receipt of income assistance as defined above.

Multinomial logistic regression assumes case-specific and non-perfect separation. We constructed a two-way tabulation of the outcome variable with each variable to check the assumption. In addition, multicollinearity between the independent variables were tested with variance inflation factors.

Analyses were conducted using SAS Enterprise Guide version 7.1 and R version 3.5.1. An alpha level of 0.05 was used for all statistical tests.

Results

The OUD cascade of care

Among 76,926 PWOUD identified within the period of data capture, we identified 55,470 diagnosed PWOUD alive and not administratively censored as of November 30th, 2017. The OUD cascade of care in BC from 2001 to 2017 is illustrated in **Figure 1**. The number of diagnosed PWOUD increased substantially from 15,972 in 2001 to 55,470 in 2017, reflecting a greater than 3-fold increase in 16 years. As of 2017, although 71% of diagnosed PWOUD had ever engaged in OAT, 33% were currently on OAT, and only 16% had been retained in care for 1 year.

Characteristics of new diagnoses

We examined characteristics of PWOUD diagnosed within 5 years of the end of study follow-up period to further investigate the growth in OUD diagnoses in BC (**Table 2**). At least 5,538 PWOUD were identified in 2016, a 27% increase from 2012. Since 2012, at diagnosis, age, sex, area of residence, setting of initial OUD-related contact, and health service utilization have remained relatively stable; however, we noted an association between year of diagnosis and each covariate investigated ($p < 0.01$); excluding HIV and HCV comorbidities. At the end of 2015, 32% of new diagnoses occurred among 25-34 year olds, most cases resided in urban areas (95%), were male (63%), and were mainly identified by either outpatient care or OAT dispensation (73%). An estimated 44% of cases identified via outpatient care had received OAT within 3 months of their diagnosis in 2015, while only 7% of cases identified by hospitalizations received OAT within 3 months of their diagnosis.

The cascade of care by region

Of the 55,470 diagnosed PWOUD, N=53,097 (96%) resided in urban regions and N=2,338 (4%) resided in rural regions of BC in 2017 (**Figure 2**). PWOUD in rural regions experienced relatively greater attrition along the cascade compared to urban PWOUD ($p < 0.001$ in each stage). Although 72% of PWOUD in urban regions had ever engaged in OAT, only 61% had ever engaged in OAT in rural regions. In subsequent stages of the cascade of care,

engagement and retention was consistently lower for rural PWOD relative to urban PWOD. This pattern was observed across the province, regardless of HSDA. Only 16% and 11% of diagnosed PWOD were retained in OAT for one year or longer among PWOD in urban and rural regions, respectively.

Cascade attrition after diagnosis and treatment engagement

Characteristics of PWOUD currently on OAT

We compared demographic characteristics among PWOUD currently on OAT to those diagnosed but never on OAT (OAT naïve), and those who had ever initiated OAT but were not currently engaged in OAT (excluding PWOUD who had completed OAT tapering) to investigate demographic factors associated with OAT engagement (**Table 3**). During the study period, 564 individuals had missing age group and sex. In addition, 52 individuals were missing region of residence. These data were considered as missing at random, conditionally on the outcome and other covariates in the regression model. In such cases, complete case analysis would not be biased(49). As a result, a total of 605 individuals (<1%) were excluded from the regression analysis, leaving a total of 62,886 individuals with 457,444 annual measurements incorporated in the multinomial model.

Compared to those never on OAT, PWOUD currently engaged in OAT were more likely to be under 45 years of age at diagnosis (adjusted odds ratio: 1.75; 95% confidence interval: 1.64,1.89), male (1.72;1.64,1.82) and with other substance use disorders (2.56; 2.44,2.70) and HCV (1.22; 1.14,1.33). They were additionally more likely to have a longer time since OUD diagnosis (1.03; 1.03,1.04) and either homeless or receiving income-assistance (4.35; 4.17,4.55), after controlling for other demographic factors.

Relative to PWOUD who had ever engaged in OAT, PWOUD currently engaged in OAT were more often between the ages of 35 to 44 at diagnosis(1.08; 95%CI:1.01,1.15), male (1.12; 1.09,1.18), with other substance use disorders (1.54; 1.47,1.61) and HIV (1.39; 1.28,1.52). Those engaged in care were also more likely to have mental health disorders (1.43; 1.35,1.49) and be either homeless or receiving income-assistance (1.69; 1.64,1.79).

Healthcare utilization among PWOUD not engaged in OAT

We further described health care use patterns among PWOUD not on OAT from April 1st 2015 to March 31st 2016 to identify potential targets for OAT induction or re-initiation (**Figure 4**). We identified a total of 14,991 PWOUD who had never engaged in OAT and 26,589 PWOUD who

had ever engaged in OAT but were not currently on OAT as of March 31st 2016. For both groups, there was an association between time since OUD diagnosis or discontinuation and type of health care service accessed ($p < 0.001$). Regardless of time since diagnosis or discontinuation, a large majority of clients not engaged in OAT were receiving at least routine outpatient care in the previous 12 months. A higher proportion of PWOUUD diagnosed or disengaged for over 12 months had no health system contact within the past year, however even within these groups, 82-91% were at least receiving low intensity outpatient care. Hospitalizations were common, particularly among those diagnosed (46%) and those who discontinued OAT (22%) within the past year.

Discussion

Since 2001, we observed a greater than three-fold increase in the number of diagnosed PWOD across British Columbia, and modest increases in OAT engagement alongside persistently low rates of retention. Leveraging the comprehensive health administrative data available in BC, the cascade of care provides a powerful framework to identify the numbers and demographic characteristics of PWOD lost to care at various points in the OUD care continuum and produce key information for future planning in provincial health policy and national strategies to address the public health emergency.

Since 2001, we identified annual increases of up to 12% in the number of PWOD who had ever initiated OAT, likely a reflection of long-standing provincial efforts to expand access to low-barrier addiction treatment(50) and engage more physicians in OUD care(51). While a majority (71%) of the population of PWOD had accessed OAT in 2017, only 33% were currently on OAT, and fewer than half of those (16%) were retained for at least one year. To address these gaps in care, the province has opened integrated care clinics(52), addiction treatment support programs(53), approved new forms of OAT(54) with new clinical guidelines(37, 55), and eliminated OAT co-payment fees for the vast majority of clients(56) in addition to most physician eligibility requirements for OAT prescription(57). However, further targeted action is needed to change the course of the epidemic and improve the cascade of care through approaches that address OUD identification, treatment engagement, and OAT initiation and retention(58).

Future efforts should focus on the engagement of individuals who are accessing care for OUD-related causes but are not receiving OAT. Treatment engagement for OUD can be improved through expansion of settings where OAT can be initiated, and enhanced care integration(58). We identified 29% of our population as OAT naïve. Furthermore, although a majority of our OUD population were identified by hospitalizations and outpatient care, only 7% and 44% of these cases respectively had received OAT within 3 months of their first OUD-related visit. Since a majority of the population were living with mental health conditions, chronic pain and other substance use disorders prior to OUD diagnosis, targeted interventions for OUD identification and treatment engagement should focus in settings providing care for these

conditions. Additionally, settings managing infectious diseases provide opportunities to engage PWOD in treatment as OUD often comes with risk of HCV and HIV infection among those who inject drugs(59, 60).

We otherwise found hospitalizations were common among those recently diagnosed or disengaged from OAT. Inpatient care settings, particularly the emergency department (ED), present promising solutions in OUD screening and OAT initiation(61). Many North American EDs have initiated buprenorphine for patients with referral to outpatient care with reported success in retention and reduction of ED visits(62, 63). Similarly, a BC pilot project is currently underway to provide ED opioid overdose patients with take-home buprenorphine/naloxone upon discharge(64).

As challenges to improve access to OAT persist in rural BC(32), it is unsurprising that we observed lower retention and engagement in PWOD located in rural regions. Remote and rural regions of BC have historically faced numerous barriers in supporting substance use-related interventions with limited infrastructure and capacity for service delivery(65). It is reported that many health care providers trained to prescribe OUD medication do not offer the treatment(66), suggesting training may not be adequate to address the shortage of providers in rural settings(58). Combatting stigma, increasing the number of pharmacies equipped for OAT dispensation and increasing reimbursement rates for OAT prescription and dispensation are noted strategies to encourage OAT access in rural areas(58). Additionally, telehealth and telementoring initiatives have been implemented locally and in other contexts such as the US, with aims to improve access to timely clinical expertise and reduce disparities across diverse geographical contexts(67, 68).

While improvements in OAT engagement were observed over the study period, low rates of retention persisted. Numerous interventions have shown promise in improving OAT retention such as use of cognitive behavioral therapy with contingency management and incentives for patients and clinicians(69). Further, a recent cohort study associated cannabis use with 21% greater odds of retention in OAT at six months(70). The importance of continuity of treatment, particularly after release from prison, and the elimination of punitive measures for concurrent

drug use are additional key factors that must be addressed to improve retention(71). However, further research is needed to determine the comparative effectiveness of OAT medications for different population subgroups, reasons for treatment discontinuation and strategies to address factors behind discontinuation(72, 73). We note the retention rates reported were determined from conservative discontinuation thresholds of 5 days for methadone and 6 days for buprenorphine/naloxone in accordance with clinical guidelines indicating the need to re-initiate clients on starting doses following absences of these durations(5). Other studies have defined this threshold at 7 and 14 days(10, 74); our figures should be interpreted with this distinction in mind.

For many PWOD, OAT is not an immediate goal. Many PWOD have a desire for abstinence, while some feel stigmatized for using OAT and are not inclined towards treatment(75). The availability of harm reduction services such as overdose prevention facilities(76), supervised consumption sites(77), naloxone kit distribution(78), drug checking services(76), outreach and peer to peer support programs(79) have all been priority interventions for PWOD choosing not to engage in treatment and represent opportunities to intervene and refer individuals to treatment and social support services as needed and appropriate(80). Future monitoring efforts may also account for access to harm reduction services to track care for PWOD otherwise not accessing services in inpatient or outpatient settings.

To date, most of the efforts in addressing OUD have focused on treatment; however, the identification and prevention of OUD are also key components of a comprehensive approach to OUD(81). Screening for OUD in all relevant health care settings as well as increasing physician and nurse training in OUD identification (particularly in individuals at high risk, for example those with other substance use disorders and those receiving high doses of prescription opioids) and treatment are instrumental to support care integration(82). The high degree of identification through inpatient settings and frequent health system contacts prior to OUD diagnosis point to unrealized opportunities for early diagnosis and treatment engagement.

We noted substantial attrition in engagement and retention stages of the OUD cascade of care. Further efforts involving increased access to alternative forms of OAT, care for target

populations, quality improvement initiatives, and peer-to-peer support, are needed to ensure sustained engagement in care and to allow re-engagement for those lost to treatment. Fewer than 3% of PWOD achieve long term remission(83, 84) and those left untreated are likely to fall victim to an overdose, further emphasizing importance in the adoption of a chronic disease model for OUD and its recognition as a treatable chronic disease, with a range of treatment options with no imposed time restrictions(58, 85).

Limitations

Despite comprehensive scope of the databases utilized, our results are reported with several limitations. First, the population was defined on the basis of health administrative data resulting in possible misclassification; however, case-finding algorithms were used to minimize misclassification. Furthermore, our administrative databases capture only service provision, rather than direct measures of accessibility; however prior reports have documented lower access to addictions care in rural regions of BC and across Canada(31,60). Third, our capture of health service was not complete - utilization of community and harm reduction services are currently only available at an aggregate-level, while capture of ED admissions was limited to those subsequently hospitalized. Further efforts to expand these database linkages to also include contacts with criminal justice and social services will provide greater context for targeted intervention. Fourth, in the regression analysis, there may be potential bias from unmeasured confounders and a coarseness in the inferences presented due to the annual measurement of treatment engagement. Additionally, interventions occurring during the study period were not adjusted for and non-linear trends were not considered. Finally, the low-threshold care model employed in BC where most forms of OAT (including both methadone and buprenorphine/naloxone) can be prescribed by primary care physicians and dispensed through community-based pharmacies may limit generalizability of our findings to settings with more stringent restrictions on OAT access(32, 86). Nonetheless, we believe this representation of the OUD cascade of care is the most comprehensive to date.

Conclusions

Through application of an OUD cascade of care framework, we identified a 247% increase in the size of the diagnosed population of PWOD from 2001 to 2017, alongside modest increases in OAT engagement. Our findings of high levels of outpatient care prior to diagnosis and several key demographic factors independently associated with OAT receipt highlight actionable opportunities for engagement in care for PWOD.

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Tables & Figures

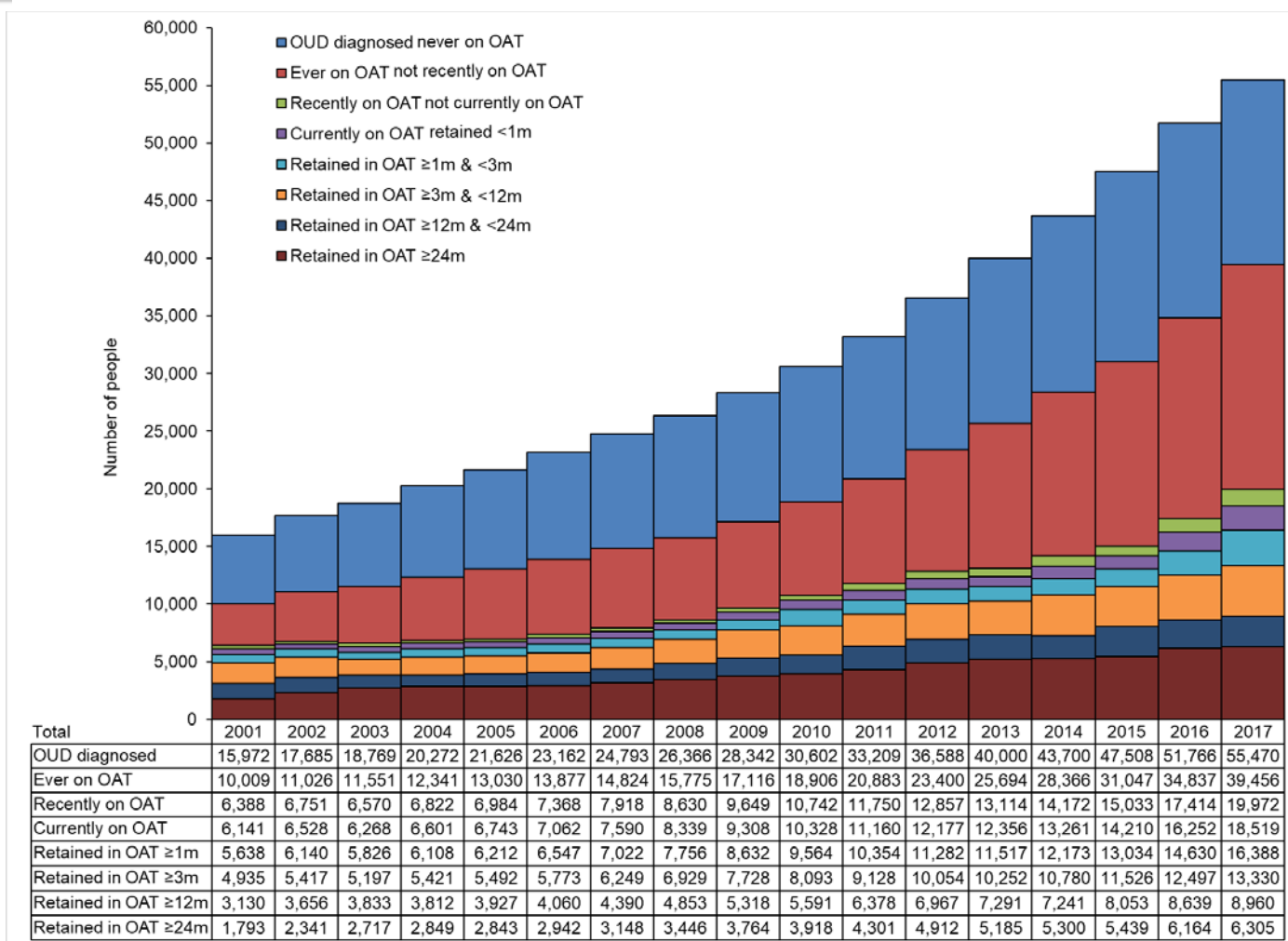
Table 1. Opioid use disorder cascade of care definitions

Cascade Stage	Definition
OUD 'diagnosed'	The first instance of one of the following: 3 OUD-related physician billing records (MSP), 1 OUD-related hospitalization (DAD) or 1 OAT drug dispensation (PharmaNet).
Ever engaged in OAT	OUD diagnosed individuals with at least one OAT dispensation record (any receipt of MET, BNX, SROM or iOAT) as of the end of follow-up (November 30, 2017) or calendar year.
Recently Engaged in OAT	OUD diagnosed individuals with OAT discontinuation occurring within ≤ 30 days as of the end of follow-up or calendar year.
Currently On OAT	OUD diagnosed individuals continuously engaged in OAT as of the end of follow-up or calendar year.
Retained in OAT $\geq 1m$	OUD diagnosed individuals continuously engaged in OAT $\geq 1m$ as of the end of follow-up or calendar year.
Retained in OAT $\geq 3m$	OUD diagnosed individuals continuously engaged in OAT $\geq 3m$ as of the end of follow-up or calendar year.
Retained in OAT $\geq 12m$	OUD diagnosed individuals continuously engaged in OAT $\geq 12m$ as of the end of follow-up or calendar year.
Retained in OAT $\geq 24m$	OUD diagnosed individuals continuously engaged in OAT $\geq 24m$ as of the end of follow-up or calendar year.

Abbreviations: MSP medical services plan; DAD discharge abstract database; OUD opioid use disorder; OAT opioid agonist treatment; MET methadone; BNX buprenorphine/naloxone; SROM slow release oral morphine; iOAT injectable opioid agonist treatment.

Continuous OAT engagement defined as a continuous period of dispensed medication with no interruptions, or 'gap times' in prescribed doses lasting < 5 days for MET or SROM, < 6 days for BNX, and < 3 days for iOAT.

Figure 1. The opioid use disorder cascade of care in British Columbia, Canada, January 1st 2001 to November 30th 2017.



Abbreviations: OUD opioid use disorder; OAT opioid agonist treatment.

Provincial counts generated at the end of each calendar year. Colored bars represent mutually exclusive stages.

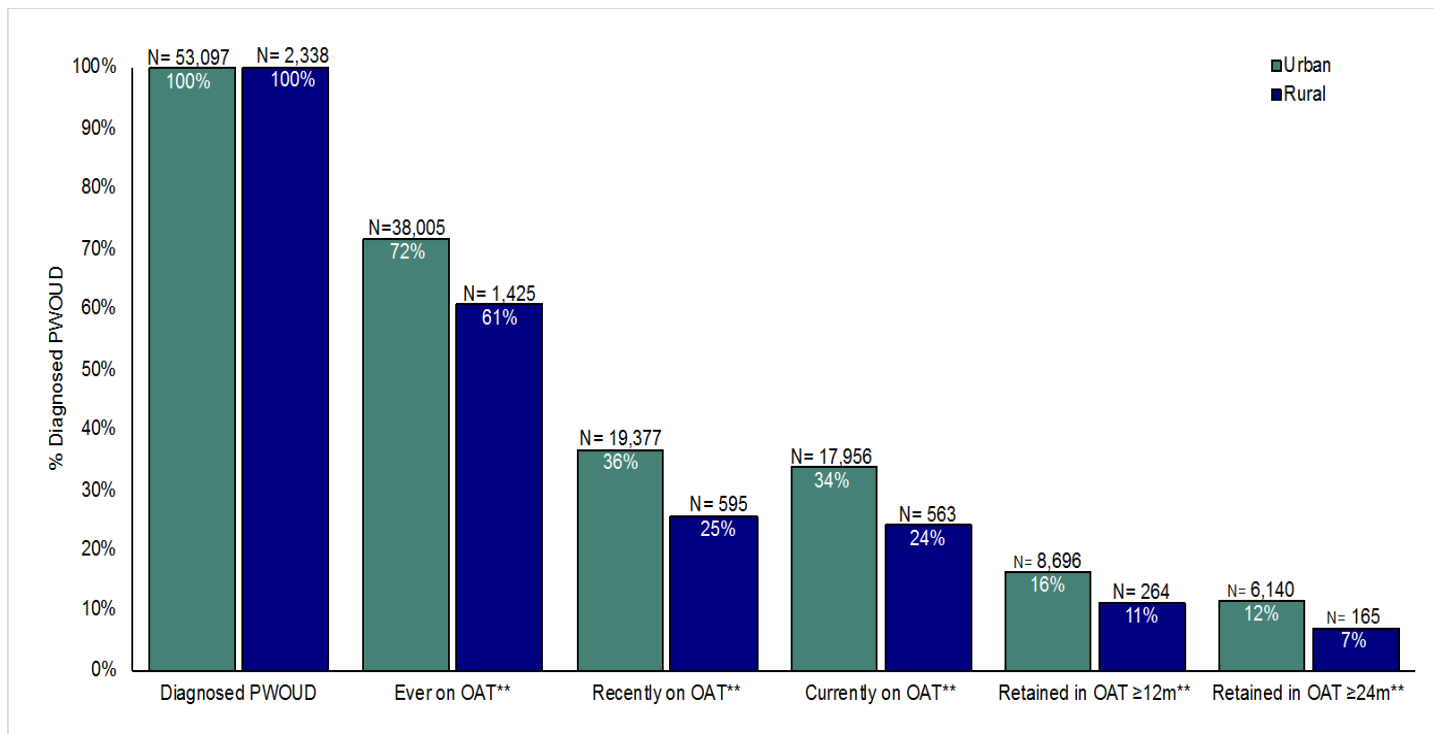
Table 2. Characteristics of newly diagnosed people with opioid use disorder in British Columbia, Canada, January 1st 2012 to December 31st 2016.

	2012	2013	2014	2015	2016 ^a	p-value*
Total	4,375	4,242	4,531	4,773	5,538	
Age [N (%)]^b						
<25 years	921 (21)	842 (20)	941 (21)	1,023 (22)	1,058 (20)	0.33
25-34 years	1,405 (33)	1,275 (31)	1,367 (31)	1,513 (32)	1,793 (34)	0.07
35-44 years	777 (18)	803 (19)	846 (19)	883 (19)	1,003 (19)	0.6
≥45 years	1,201 (28)	1,239 (30)	1,301 (29)	1,239 (27)	1,498 (28)	0.15
Residence [N (%)]^c						
Rural	234 (5)	256 (6)	269 (6)	221 (5)	212 (4)	<0.01
Urban	4,135 (95)	3,979 (94)	4,255 (94)	4,544 (95)	5,321 (96)	
Sex male [N (%)]^d						
	2,673 (62)	2,530 (61)	2,818 (63)	2,948 (63)	3,427 (64)	<0.01
Basis of identification [N (%)]						
Hospital	1,294 (30)	1,351 (32)	1,338 (30)	1,558 (33)	1,782 (32)	<0.01
Received OAT within 3 months of diagnosis	60 (5)	84 (6)	86 (6)	107 (7)	168 (9)	<0.01
Physician billing	1,008 (23)	1,095 (26)	1,188 (26)	1,244 (26)	389 (7)	<0.01
Received OAT within 3 months of diagnosis	412 (41)	367 (34)	427 (36)	551 (44)	171 (44)	<0.01
OAT dispensation	2,210 (51)	1,959 (46)	2,196 (48)	2,224 (47)	3,444 (62)	<0.01
Comorbidities prior to OUD diagnosis [N (%)]						
Substance use disorder	2,094 (48)	1,980 (47)	1,968 (43)	2,032 (43)	1,783 (32)	<0.01
Alcohol use disorder	850 (19)	793 (19)	838 (18)	947 (20)	992 (18)	0.24
HIV	56 (1)	29 (1)	49 (1)	48 (1)	53 (1)	0.48
HCV	133 (3)	111 (3)	98 (2)	120 (3)	150 (3)	0.37
Mental health disorder	3,079 (70)	2,985 (70)	3,124 (69)	3,153 (66)	3,413 (62)	<0.01
Chronic pain	2,556 (58)	2,482 (59)	2,558 (56)	2,526 (53)	2,740 (49)	<0.01
Health service utilization one year prior to OUD diagnosis [N (%)]						
No contact	596 (14)	581 (14)	649 (14)	714 (15)	945 (17)	<0.01
Outpatient care only - low intensity	2,212 (51)	2,067 (49)	2,219 (49)	2,398 (50)	2,860 (52)	0.08
Outpatient care only - high intensity	572 (13)	569 (13)	547 (12)	516 (11)	504 (9)	<0.01
1 hospitalization	563 (13)	553 (13)	587 (13)	603 (13)	653 (12)	0.07
>1 hospitalization	432 (10)	472 (11)	529 (12)	542 (11)	576 (10)	0.49

Abbreviations: OUD opioid use disorder; OAT opioid agonist treatment; HIV human Immunodeficiency virus; HCV hepatitis C virus
a. Physician billing records (MSP) recorded only until March 31, 2016; b. Age defined as age at end of calendar year; c. N=39 region of residence unknown; d. N=638 sex and age unknown; e. Low intensity outpatient care defined as having both all cause physician billing records (medical services plan MSP) and all cause drug dispensation days (PharmaNet) < the 75th percentile (Q3), High intensity outpatient care: having *either* all cause physician billing records *or* all cause drug dispensation >Q3, Q3 determined from all PWOD

diagnosed during 2012 to 2016 one year prior to OUD diagnosis (Q3 MSP= 49; Q3 PharmaNet= 1,332). * Determined via Cochran-Armitage test for temporal trends.

Figure 2. The opioid use disorder cascade of care among urban and rural dwellers in British Columbia, Canada, as of November 30th 2017.



Abbreviations: PWOD people with opioid use disorder; OAT opioid agonist treatment.

** Statistical significance $p < 0.001$ determined via chi-squared test comparing urban vs. rural proportion of PWOD in each cascade stage. N=35 individuals with unknown geographic location excluded

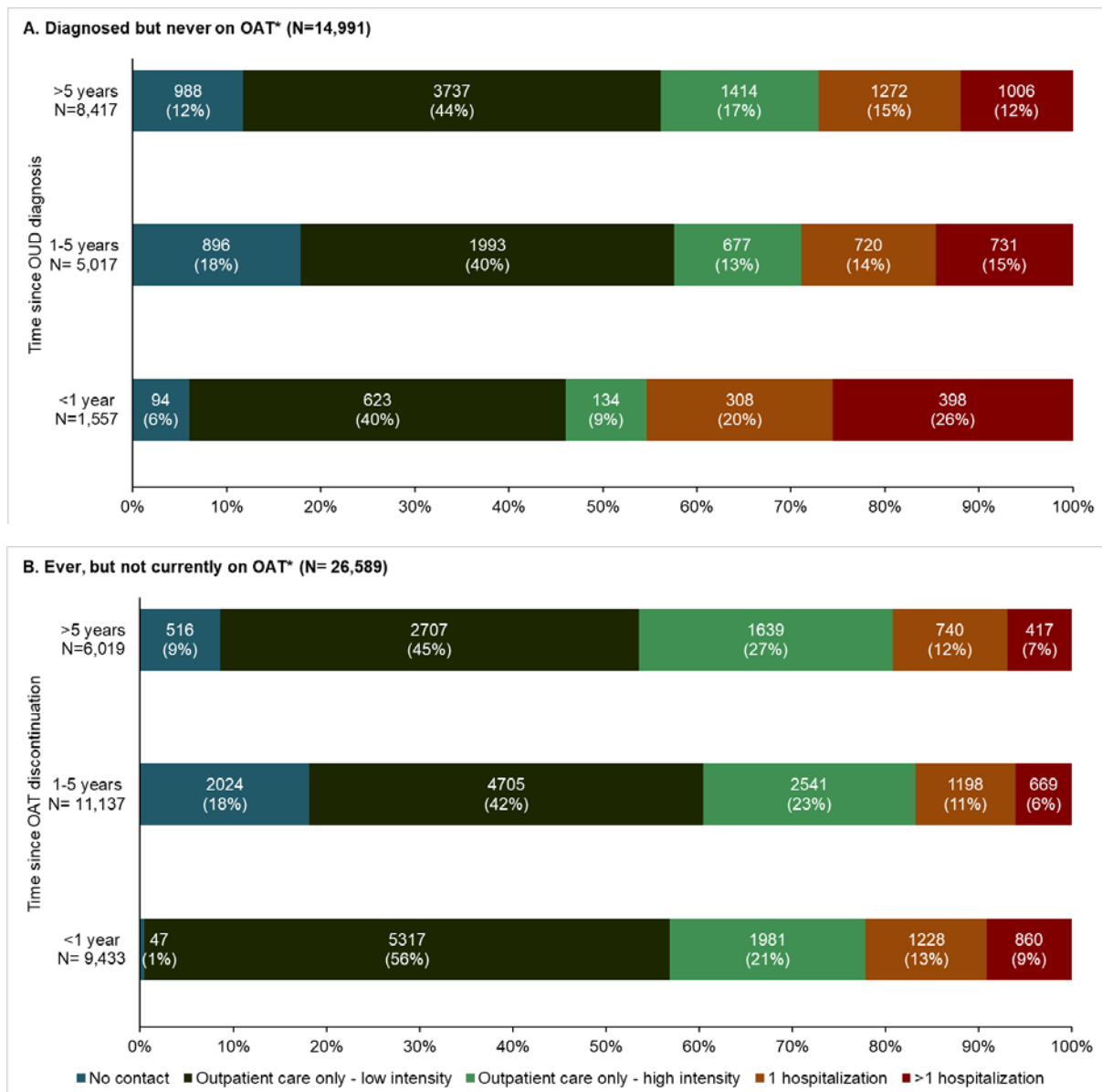
Table 3. Crude and adjusted GEE analyses of demographic factors associated with OAT engagement in British Columbia, Canada, January 1st 2001 to December 31st 2016 (N=62,886[^]).

Characteristic	Those currently on OAT versus those diagnosed, but never on OAT		Those currently on OAT versus those ever but not currently on OAT	
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
<i>Age group at OUD diagnosis (ref: ≥45 years)</i>				
<25 years	2.56 (2.38, 2.78)	1.79 (1.67, 1.92)**	0.93 (0.86, 1.02)	0.86 (0.81, 0.92)**
25-34 years	2.94 (2.70, 3.13)	2.04 (1.89, 2.17)**	0.96 (0.88, 1.03)	0.88 (0.83, 0.93)**
35-44 years	2.56 (2.33, 2.78)	1.75 (1.64, 1.89)**	1.20 (1.12, 1.32)	1.08 (1.01, 1.15)*
Male sex (ref: female)	1.61 (1.54, 1.69)	1.72 (1.64, 1.82)**	1.04 (1.01, 1.09)	1.12 (1.09, 1.18)**
Rural residence ¹ (ref: urban)	0.36 (0.33, 0.40)	0.49 (0.44, 0.54)**	0.56 (0.51, 0.62)	0.60 (0.54, 0.66)**
<i>Comorbidities[†] (ref: no comorbidity)</i>				
Other substance use disorders	3.13 (2.94, 3.23)	2.56 (2.44, 2.70)**	1.89 (1.82, 2.00)	1.54 (1.47, 1.61)**
Alcohol use disorder	0.52 (0.50, 0.55)	0.36 (0.35, 0.38)**	1.03 (0.99, 1.08)	0.84 (0.8, 0.88)**
HIV	1.69 (1.54, 1.85)	0.97 (0.88, 1.08)	1.67 (1.52, 1.82)	1.39 (1.28, 1.52)**
HCV	1.39 (1.30, 1.49)	1.22 (1.14, 1.33)**	1.27 (1.19, 1.35)	1.00 (0.93, 1.06)
Mental health disorder	0.88 (0.84, 0.93)	0.71 (0.67, 0.76)**	1.72 (1.67, 1.82)	1.43 (1.35, 1.49)**
Chronic pain	0.68 (0.65, 0.70)	0.64 (0.60, 0.67)**	1.20 (1.15, 1.25)	0.95 (0.92, 0.99)*
Calendar-years since OUD diagnosis	1.06 (1.05, 1.06)	1.03 (1.03, 1.04)**	1.02 (1.02, 1.02)	1.00 (1.00, 1.01)
Ever homeless or income-assistance enrollment ¹ (ref: never homeless and not enrolled in income-assistance)	4.76 (4.55, 5.00)	4.35 (4.17, 4.55)**	1.96 (1.89, 2.04)	1.69 (1.64, 1.79)**

Abbreviations: GEE: generalized estimating equations; OR: odds ratio; AOR: adjusted odds ratio; OAT opioid agonist treatment; HIV human Immunodeficiency virus; HCV hepatitis C virus; OUD opioid use disorder. [^]period prevalence – including those dying or lost to follow-up prior to December 31st 2016. ¹Determined at the end of each calendar year. *0.01 ≤ p < 0.05; **p < 0.01.

N=605 individuals missing age, sex and/or geographic data excluded from model.

Figure 3. Health care utilization among individuals with opioid use disorder not engaged in opioid agonist treatment in British Columbia, Canada, from April 1st 2015 to March 31st 2016.



Abbreviations: OUD opioid use disorder; OAT opioid agonist treatment

a. For PWOUD diagnosed or discontinued OAT <1 year, OUD-related records on date of OUD-diagnosis/OAT discontinuation excluded. * Statistical significance $p < 0.001$ from Chi-squared tests of independence between time since diagnosis or discontinuation and health care utilization categories. Low intensity outpatient care defined as having both physician billing records (medical services plan MSP) and drug dispensation days (PharmaNet) < the 75th percentile (Q3); High intensity

outpatient care: having *either* physician billing records or drug dispensation >Q3. Q3 determined from all PWOD alive as of March 31st 2016. Physician billing records and drug dispensation days from April 1st 2015 to March 31st 2016 (Q3 MSP= 102; Q3 PharmaNet= 1,609). N=2,149 PWOD who completed OAT tapering excluded from PWOD ever but not currently on OAT group (Panel B).



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